In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 16-867V

(to be published)

* *	Chief Special Master Corcoran
KAYLON TIPPS, *	
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Petitioner, *	
*	
*	Dated: December 9, 2022
v. *	
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SECRETARY OF HEALTH AND *	
HUMAN SERVICES, *	
*	
Respondent. *	
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* *	

John R. Howie, Jr., Howie Law P.C., Dallas, TX, for Petitioner.

Jennifer L. Reynaud, U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On July 22, 2016, Kay and Cathell Tipps, on behalf of their minor son, Kaylon (referred to as 'K.T." at the time of filing, but now the named Petitioner)[2] filed a petition for compensation under the National Vaccine Injury Compensation Program (the "Program").[3] Petition (ECF No. 1)

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] Mr. Tipps became the Petitioner when he turned 18, and the caption was accordingly amended. See Order, dated May 4, 2022 (ECF No. 82).

[3] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

("Pet.") at 1. Petitioner alleges that Meningococcal and Tetanus-Diphtheria-Acellular-Pertussis ("Tdap") vaccines he received on July 24, 2013, caused him to suffer meningitis and seizures.

A two-day entitlement hearing in the matter was held in Washington, D.C. on May 4–5, 2022. Having reviewed the record, all expert reports and associated literature, and listened to the testimony at hearing, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not preponderantly established that the Meningococcal and Tdap vaccines were likely causal of his subsequent illness.

I. Fact History

Vaccination and Six-Month Period Thereafter

Mr. Tipps was born on May 31, 2001. *See* Ex. 2 at 3. Prior to the vaccinations at issue, he was in good health, and his medical history only establishes the existence of asthma, allergies, eczema, and obesity. *Id*. at 4. On July 24, 2013, Petitioner (then twelve years old) received Meningococcal and Tdap vaccines from his primary care physician. *Id*. at 5–6. The record does not indicate that he experienced any immediate adverse reactions following the administration of either vaccine.

On August 9, 2013 (sixteen days after his vaccinations), Petitioner was taken to the emergency room ("ER") at Crescent Medical Center complaining of a throbbing headache that had persisted for over two hours. Ex. 3 at 5. His parents reported that in addition to the severe headache, he was experiencing blurred vision. *Id*. at 5, 8. Upon examination, the treating physician concluded that Mr. Tipps was dehydrated, and he was given fluids via an IV, pain medication, and discharged home thereafter. *Id*. at 10.

Three days later (and shortly after midnight), on August 12, 2013, Mr. Tipps returned to the ER at Crescent Medical Center due to episodes of starring and unresponsiveness accompanied by a severe headache and projectile vomiting. Ex. 3 at 20. It was reported that his symptoms began three days prior, and that he had started experiencing intense neck pain and vision changes. *Id*. On exam, the treating physician observed erythema in Petitioner's tympanic membranes,[4] and prescribed anti-seizure medication and antibiotics due to the concern for a central nervous infection. *Id* at 21. Petitioner then underwent a CT scan of his head, the results of which were unremarkable. *Id*. at 31. Before being transferred to Children's Medical Center for further evaluation, Mr. Tipps's initial differential diagnosis included seizure disorder and mental status change, with encephalitis ruled out. *Id*. at 21.

[4] "Tympanic Membrane," is defined as "the obliquely placed, thin membranous partition between the external acoustic meatus and the tympanic cavity." *Membrana Tympanica*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=88565 (last visited Dec. 9, 2022).

Petitioner arrived at the ER at Dallas Children's Hospital around 4:00 a.m., on August 12, 2013. Ex. 4 at 1. There, his parents reported that he had been acting strangely the last three days, recounting his ER visits at Crescent Medical Center and noting that he had a cough, runny nose, and symptoms of an upper respiratory infection. *Id*. at 5. After undergoing a lumbar puncture, Mr. Tipps's cerebral spinal fluid ("CSF") analysis revealed pleocytosis.[5] Petitioner's treating physicians felt this finding (coupled with his overall presentation) was consistent with a viral meningoencephalitis[6] that was resolving. *Id*. at 25. However, because the CSF sample was obtained in a setting in which Petitioner was receiving certain medications that might impact the result, the CSF analysis was ultimately deemed unreliable. *Id*. at 27. Petitioner was discharged the following day with a diagnosis of aseptic versus viral meningitis. Ex. 4 at 27.

On August 20, 2013, Petitioner saw pediatric neurologist, Dr. Kazi Majeed, at which time he and his parents reported a history of prolonged, intermittent staring and unresponsiveness since August 9th. Ex. 5 at 1. Following examination, a CT scan and an EEG were performed, both of which resulted in normal findings— leading Dr. Majeed to propose that Mr. Tipps's symptoms reflected partial complex seizures. *Id*. at 3. Dr. Majeed recommended that Petitioner undergo a 48-hour ambulatory VEEG[7] to try and determine a cause for the staring spells and unresponsiveness. *Id*. at 3

On August 29, 2013, Mr. Tipps saw pediatric neurology physician's assistant, Michelle Ashcraft, PA, at the Headache Specialty Clinic at Children's Medical Center. Based on physical examination, recent hospitalization, and ongoing symptoms, PA Ashcraft recommended that Petitioner be admitted to Children's Medical Center for further neurologic evaluation, viral studies, a brain MRI, and a possible lumbar puncture. Ex. 4 at 168–73.

The subsequently-performed lumbar puncture revealed elevated intracranial pressure (opening pressure of 55 and a closing pressure of 19), and the brain MRI showed evidence of

[5] "Pleocytosis" is defined as the "presence of a greater than normal number of cells in the cerebrospinal fluid." *Pleocytosis*, Dorland's medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39556 (last visited Dec. 9, 2022).

[6] "Meningoencephalitis," is defined as "inflammation of the brain and meninges." *Meningoencephalitis*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=30351&searchterm=meningoencephalitis (last visited Dec. 9, 2022).

[7] An electroencephalogram (EEG) is a test that involves placing small metal discs, also known as electrodes, on an individual's scalp, in order to detect electrical brain abnormalities. A video electroencephalogram (VEEG) on the other hand, is known as a more specialized form of an EEG, but includes the constant video monitoring of the individual throughout the testing period. *The VEEG (Video Electroencephalogram) Test Appears Useful for Identifying Seizures*, Brain Injury Association of America, https://www.biausa.org/professionals/research/tbi-model-systems/the-veeg-video-electroencephalogram-test-appears-useful-for-identifying-seizures (last visited Dec. 9, 2022).

papilledema, consistent with the increased pressure.[8] Ex. 4 at 186. Petitioner was prescribed medication for the elevated intracranial pressure and his headaches. *Id*. In addition, he was evaluated by an infectious disease specialist who ruled out enterovirus, West-Nile, Arbovirus, Varicella, and Herpes Simplex Virus ("HSV") as potential causes for his symptoms. *Id*. at 186, 188. Petitioner remained at Children's Medical Center until September 2, 2013, when his treating physicians determined that he was stable enough for discharge. At that time, he was diagnosed with headache, pseudotumor cerebri,[9] and aseptic meningitis. *Id*. at 184. Petitioner was advised to follow up with neurology and ophthalmology consults. *Id*. at 190.

Petitioner was taken to the ER at Methodist Charlton Medical Center on September 4, 2013, after complaining of neck pain and worsening headaches. Ex. 4 at 665. But because of his complicated history, he was transferred to Dallas Children's for further evaluation, where (after his intracranial pressure medication dosage was adjusted) the severity of his symptoms subsided, and he was later discharged. *Id*. at 667, 670. Then, on September 6, 2013, Mr. Tipps saw Dr. Majeed who performed an EEG, the results of which indicated abnormal activity consistent with encephalopathy, although no seizure activity was observed at this time. Ex. 5 at 4.

After experiencing worsening headaches and neck and back pain, Petitioner returned to the ER on September 8, 2013, and was subsequently admitted to Medical City Dallas Hospital ("MCDH"). Ex. 5 at 23. Upon admittance, he underwent another lumbar puncture which revealed elevated intracranial pressure, and decreased sodium levels in the sample as well as his blood. *Id.* at 47, 63. Extensive CSF studies for various possible causative agents were performed, and even though all produced negative results, the infectious disease consultant opined that the etiology of Mr. Tipps's condition was nevertheless likely due to an infection "given his pleocytosis of lymphocytosis." *Id*. at 23. In addition to a hematology and oncology consult, Mr. Tipps was examined by a neurologist who determined that his previous diagnosis of pseudotumor cerebri from Children's Medical Center was questionable, leading him to discontinue a diuretic and initiate treatment with IV steroids. Ex. 7 at 55–56.

On September 13, 2013, Petitioner was experiencing significant deterioration in his vision. During a consult with an ophthalmologist, he was now unable to make out any details or objects, reporting that he could only see black despite the lights being on. Ex. 7 at 48–49. The ophthalmologist noted that Petitioner's pupils were not only significantly more dilated, but that

[8] "Papilledema" is defined as "edema of the optic disk (papilla), most commonly due to increased intracranial pressure, malignant hypertension, or thrombosis of the central retinal vein." *Papilledema*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=36673&searchterm=papilledema (last visited Dec. 9, 2022).

[9] "Pseudotumor Cerebri" is defined as "a condition of raised intracranial pressure with normal cerebrospinal fluid, in the absence of an intracranial mass, hydrocephalus, or other identifiable cause; symptoms include headache, nausea, vomiting, papilledema, and sometimes pulsatile tinnitus." *Pseudotumor Cerebri*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=100755&searchterm=pseudotumor+cerebri (last visited Dec. 9, 2022).

they were extremely sluggish and minimally reactive. *Id*. After consulting with other specialists and Mr. Tipps's family, arrangements were made for him to undergo an optic nerve sheath fenestration in his right eye to alleviate the pressure around his optic nerve, and to return to MCDH for further evaluation and care. *Id.* at 49. Dr. Zev Shulkin, a neuro-ophthalmologist, performed the surgery that day, noting that it was necessary for him to undergo such a surgery at that time due to the severe visual filed loss and visual acuity loss in that eye. *Id*. at 21.

Upon his return to MCDH, Mr. Tipps reported that his vision in his left eye had improved, but that he did not want to open his right eye due to a burning sensation. Ex. 7 at 16. He also complained of ongoing headaches which interfered with his ability to sleep. *Id*. A physical exam was performed which indicated drainage and photophobia in both eyes, dilated and minimally reactive pupils with swelling and slight sanguineous tearing. *Id*. Treating physicians determined that he had likely experienced vision loss and impairment secondary to elevated intracranial pressure, CF pleocytosis, peripheral leukocytosis, and thrombocytosis. *Id*. at 18. To address these concerns, Petitioner underwent two lumbar punctures over the next two days, the last of which showed an opening pressure of 27 and a closing pressure of less than 9. *Id*. With the hope of alleviating some of the CSF pressure, he was restarted on certain medications. *Id*.

By September 16, 2013, Petitioner's visual acuity in his left eye had become significantly impaired, leading treaters to propose that he undergo another optic nerve sheath fenestration (although this time in the left eye). Ex. 8 at 3–4. Dr. Shulkin performed the procedure, and following its completion Petitioner was transferred back to MCDH for further evaluation and care. *Id*. Despite the improvements in his right eye, Mr. Tipps remained unable to fully lateralize externally in his right eye, indicating a persistent sixth nerve palsy. Ex. 7 at 12. Repeat lumbar punctures were performed over the next several days, and by September 22, 2013, Petitioner's visual acuity exam and sixth nerve palsy showed significant improvement, resulting in him being stable enough for discharge. *Id*. at 5. He left the hospital with diagnoses of increased intracranial pressure, aseptic meningitis, severe papilledema, and improved vision loss. *Id*. at 1.

Treatment in 2015 to Present

There is a subsequent two-year records gap, revealing no treatment for Petitioner until December 16, 2015, when he was evaluated by rheumatologist Dr. Maria Perez for his "persistently elevated inflammatory markers over the past two years." Ex. 10 at 312. Following an extensive work-up, Dr. Perez opined that there was no evidence to suggest he suffered from a rheumatic, autoimmune, or immunodeficiency illness. *Id*. at 61. Additional testing also revealed no evidence of a mass or lymphadenopathy in his chest, abdomen, or pelvis. *Id*.

However, because of his elevated ESR/CRP, Petitioner was referred to pediatric oncologist, Dr. Neethu Menon, due to concern for lymphoproliferative disorder. Ex. 12 at 1–4.

Following an exam and review of his labs, Dr. Menon opined that there was no evidence supporting a lymphoproliferative disorder diagnosis. *Id*. at 5. She did, however, note the severity of his vision impairment in his right eye, that his pupils showed impaired light reaction, and that his optic nerve was impaired bilaterally. *Id*. at 8.

During a re-evaluation with Dr. Shulkin approximately six months later (on June 8, 2016), Petitioner's visual acuity was reported as 20/50 (-2) on the right and 20/20 on the left. Ex. 8 at 28. At a later visit on October 31, 2016, his visual acuity was 20/40 on the right and 20/20 on the left. *Id*. However, despite such improvements, Petitioner continues to have significant ongoing health-related issues—suffering from regular headaches and general vision impairment. Ex. 1 ¶ 24.

II. Hearing Testimony

A. *Petitioner's Fact Witnesses*

1. Kaylon Tipps

Petitioner was the first witness to testify at the hearing. *See generally* Tr. at 6–13. He provided a brief overview of his academic studies and achievements, the extracurricular activities he partakes in, and his plans following graduation. *Id.* at 6–9. He then discussed the facts and circumstances leading up to his initial hospitalization, and the symptoms he continues to suffer from as a result of his illness. *Id*. at 9–12.

Mr. Tipps recalled in particular that August 9, 2013, was very hot, and that he had been playing out in the sun for several hours with friends. Tr. at 9–10. Aside from the asthma, allergies, and eczema he had experienced pre-vaccination, he did not recall being sick with any sort of upper respiratory infection on that date. *Id*. 10–11. Indeed, he maintained that had he been sick with an upper respiratory infection, his mom would have wanted him to stay inside. *Id*. at 11. Petitioner concluded his testimony with a brief overview of his current physical health and the problems he continues to experience, noting that he remains partially blind in his right eye, he has diabetes insipidus, and that the increased pressure on his brain occasionally causes him to hear "a thundering sound." *Id*. at 12.

2. Mr. Cathell Tipps

Petitioner's father also provided live testimony. *See generally* Tr. at 14–29. He offered a brief overview of Petitioner's underlying health conditions prior to vaccination and at the time he got sick. *Id*. at 16. Before the vaccination, Petitioner had suffered from asthma, allergies, and eczema, but only took medicine as needed. *Id*. at 17. He recalled that Petitioner showed no signs of an upper respiratory infection prior to his first hospitalization—and had he been suffering from one, he would not have been permitted to play outside in the heat on August 9, 2013. *Id*. at 18–19.

He also discussed Petitioner's first hospitalization, explaining he and his wife grew concerned for Petitioner after they noticed he was not as responsive as he usually was, and that he began "starring into space." *Id*. at 19. He noted, however, that hospital staff evaluating Petitioner had seemed to conclude that he might have been dehydrated from being out in the sun all day. *Id*. at 22.

On the morning of August 12, 2013, Mr. and Mrs. Tipps took Petitioner back to the emergency room due to his unresponsiveness and persistent headaches. Again, Petitioner's father did not recall doing anything out of the ordinary the days prior to the hospitalizations, nor did he recall Petitioner suffering from an upper respiratory infection. Tr. at 24. Later, Petitioner needed to be transferred to a different hospital because Medical City did not have the proper equipment to perform a spinal tap at the time. *Id*. at 25. Following his transfer, the spinal tap was performed to alleviate some of Petitioner's pain. *Id*. at 27. Petitioner continues to experience persistent headaches and rarely wants to go outside and be active. *Id*.

B. *Petitioner's Expert Witnesses*

1. Dr. Steven Lovitt, M.D.

Dr. Lovitt, a neurologist, submitted two expert reports and testified for Petitioner. *See generally* Tr. at 30–96; Report, dated Feb. 5, 2018, filed as Ex. 14 (ECF No. 24-1) ("Lovitt First Rep."); Report, dated July 23, 2018, filed as Ex. 37 (ECF No. 32-1) ("Lovitt Second Rep.").

Dr. Lovitt received his undergraduate degree from the University of Texas, and his medical degree from Baylor College of Medicine. *See* Curriculum Vitae, filed Feb. 5, 2018 (ECF No. 24-2) ("Lovitt CV") at 1; Tr. at 31–32. After the completion of his fellowship in neuromuscular diseases in 2001, Dr. Lovitt became an Assistant Professor of Medicine and Pathology at the University of Texas Health Science Center at San Antonio, until early 2003. Lovitt CV at 2; Tr. at 32. Since then, Dr. Lovitt has been in private practice as a neurologist at The Neurology Center in Houston, TX, and has extensive experience with the diagnosis and treatment of conditions such as meningitis. *Id*. He is board certified in Neurology and Neuromuscular Medicine. Lovitt CV at 1.

Dr. Lovitt began his testimony with a brief overview of Petitioner's diagnosis. He opined that Mr. Tipps had suffered meningoencephalitis, with his initial headaches and unresponsive episodes as reflecting a seizure. Tr. at 41. In so proposing, Dr. Lovitt spent some time defining both encephalitis and meningitis, as well as discussing their diagnostic criteria.

Encephalitis, Dr. Lovitt explained, is inflammation of the brain and is generally associated with an altered mental state and cognition persisting over 24 hours, plus some other abnormality (i.e., abnormal spinal fluid with inflammatory cells or abnormal brain imaging). Tr. at 39–40. Meningitis, by contrast, is inflammation of the coverings of the brain (the "meninges"). *Id*. at 40. Meningitis is typically accompanied by a fever, stiff neck, confusion, or headache. *Id*. Dr. Lovitt

also explained that the diagnostic criteria for encephalitis and meningitis do not differ among children and adults, because "the grounds for diagnosis are based on observation and based on laboratory and ancillary testing, not [] on the age of the patients." *Id*. at 36.

Dr. Lovitt next discussed the basis for his opinion that a meningoencephalitis diagnosis was most appropriate, based on the information provided in the medical records. He first looked at the spinal taps performed on Petitioner throughout his multiple hospitalizations, emphasizing that each reading established an abnormal inflammatory process taking place within the brain. Tr. at 44. In addition, Mr. Tipps also presented with a headache and an altered mental state—thus exhibiting several of the main criteria for meningitis as defined by Dr. Lovitt. *Id*. While Dr. Lovitt noted that Mr. Tipps exhibited several features indicative of encephalitis (i.e., abnormal EEG and neuroimaging), his overall clinical presentation appeared to be more consistent with meningitis. *Id*. at 45.

Mr. Tipps's treating physicians were able to rule out a diagnosis of bacterial meningitis based on the multiple spinal taps performed, all of which found no bacteria on the cultures. Tr. at 49; Ex. 4 at 186, 209, 213, 216. Moreover, Petitioner's glucose levels were well within normal range (inconsistent with a bacterial meningitis). And while Mr. Tipps was initially treated with antibiotics (common when bacterial meningitis is suspected), he was never officially diagnosed with bacterial meningitis, and his treating physicians ceased this course of treatment as soon as it was determined that his clinical presentation did not fit such a diagnosis. Tr. at 49–50, 54. Thus, Dr. Lovitt opined that Mr. Tipps more likely than not suffered from aseptic meningitis. *Id*.

Dr. Lovitt next explained that there are two types of aseptic meningitis: noninfectious and infectious. Tr. at 51. Infectious aseptic, or nonbacterial meningoencephalitis, generally implies the existence of a viral cause, like enterovirus, although there are numerous other possibly causal viruses. Tr. at 55. Noninfectious meningoencephalitis, by contrast, can be attributable to primary illness like cancer, an autoimmune condition that manifests due to an underlying rheumatologic condition, or one that is confined exclusively to the central nervous system (the "CNS"). Tr. at 56. Dr. Lovitt noted that there are different tests physicians can conduct in order to help identify the type of aseptic meningoencephalitis an individual is suffering from. Tr. at 57. Two such common tests are PCR[10] and antibody testing.

In Mr. Tipps's case, extensive testing was performed to identify the presence of a virus—including enterovirus, arbovirus, varicella virus, West Nile virus, HSV, and EBV—all of which produced negative results. Tr. at 58; Lovitt First Rep. at 3; Lovitt Second Rep. at 3. While there was no evidence in the medical records or the test results indicating that Mr. Tipps had a viral

[10] PCR, or "Polymerase Chain Reaction," is defined as "a type of rapid nucleic acid amplification of specific DNA or RNA sequences, allowing small quantities of short sequences to be analyzed without cloning: oligonucleotide primers are annealed to single-stranded nucleotide sequences, which are copied by polymerase; the number of copies is geometrically amplified by repeated cycles of annealing and copying." *Polymerase Chain Reaction*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=102447 (last visited Dec. 9, 2022).

infection, Dr. Lovitt acknowledged that Mr. Tipps's treating physicians had reported two symptoms associated with such an infection. Tr. at 58. In particular, a facial rash was documented by treating physicians when Petitioner presented to the ER on August 12, 2013, but which was later thought to be a manifestation of heat rash, and a cough which was described as an upper respiratory infection (but never discussed further and ultimately dismissed). *Id*.

Thus, based on Mr. Tipps's clinical presentation and in reviewing the medical records, Dr. Lovitt opined that Mr. Tipps's symptoms did not likely have a viral etiology. Tr. at 61. Dr. Lovitt also deemed the unusual time course of Mr. Tipps's symptoms, and his severe increased intracranial pressure accompanied by seizures, as major factors weighing against a viral cause. Tr. at 62–63. In Dr. Lovitt's opinion and experience, cases of viral meningitis resolved within a week or two, but Mr. Tipps's symptoms had atypically lasted well over a month. Tr. at 65.

Dr. Lovitt next discussed the implications of an individual suffering from increased intracranial pressure, and how that fit in with his overall opinion that Mr. Tipps more likely than not suffered from a noninfectious form of meningoencephalitis. When an individual is suffering from increased intracranial pressure, the consequences can be severe—the pressure can sometimes push on the back of one's optic nerve which can lead to vision loss, it can push on other nerves and cause sixth nerve palsy, or it can even push the brain outside of the skull leading to herniation which can be fatal. Tr. at 76–77. Mr. Tipps's intracranial pressure was measured throughout the course of his treatments and hospitalizations, and repeatedly found to be severely elevated. *Id.*[11] As a result, Mr. Tipps's treating physicians briefly considered the possibility of a pseudotumor cerebri being the underlying cause of his symptoms, but the significant abnormal inflammation he was also displaying was not consistent with that diagnosis. *Id*. at 68. Instead, his treating physicians recommended that Mr. Tipps undergo an optic nerve fenestration to help alleviate the pressure and prevent permanent vision loss. *Id*. at 78.

Dr. Lovitt concluded his testimony by reiterating why he had concluded that Mr. Tipps's vaccinations were more likely than not the cause of his meningoencephalitis. Tr. at 83–85. Mr. Tipps had presented with a CNS inflammatory response that was accompanied with significant increased intracranial pressure, disc edema, vision loss, and spinal fluid that demonstrated the presence of an inflammatory process. *Id*. Extensive testing had been performed to identify the presence of a viral or infectious process, yet all results were negative, and there was no other evidence in Mr. Tipps's medical records or clinical presentation to suggest that he was suffering from such a process (although Dr. Lovitt admitted that negative results did not necessarily exclude the possibility of a viral or infectious cause). *Id*. at 84. Dr. Lovitt strongly opined that Mr. Tipps's clinical course was rather atypical, based on his reviewing of the medical records as well as his experience. *Id*. at 85; Lovitt Second Rep. at 3. And no other alternative explanation existed,

[11] Dr. Lovitt noted that normal pressure should typically be under 20, but Mr. Tipps's ranged from 55-90. Tr. at 68.

increasing (in Dr. Lovitt's estimation) the possibility of the vaccinations received being the cause of Mr. Tipps's meningoencephalitis. Tr. at 89; Lovitt Second Rep. at 5.

The biggest contributing factor to Dr. Lovitt's opinion that Mr. Tipps's vaccinations were causal of his meningoencephalitis was the timeframe in which his symptoms began. Tr. at 85; Lovitt Second Rep. at 3–4. Looking at the time course of Mr. Tipps's symptoms (headache, photophobia, vision changes, and unresponsiveness), an onset of 16 days post-vaccination was well within the expected timeframe to support a vaccine association. Lovitt First Rep. at 4; Lovitt Second Rep. at 5; H. Torisu et al., *Clinical Study of Childhood Acute Disseminated Encephalomyelitis, Multiple Sclerosis, and Acute Transverse Myelitis in Fukuoka Prefecture, Japan*, 32 Brain & Development 454, 457 (2010), filed as Ex. 48 (ECF No. 34-1) (finding the mean onset of neurological symptoms following vaccination was 17.7 days). Moreover, Mr. Tipps suffered from severe increased intracranial pressure for over a month—atypical for viral meningoencephalitis. *Id*. at 65.

2. Dr. David Axelrod, M.D.

Dr. Axelrod, an immunologist, submitted four expert reports and testified for Petitioner. *See generally* Tr. at 101–58; Report, dated July 23, 2018, filed as Ex. 25 (ECF No. 29) ("Axelrod First Rep."); Report, dated Sept. 6, 2019, filed as Ex. 52 (ECF No. 42-1) ("Axelrod Second Rep."); Report, dated Mar. 5, 2021, filed as Ex. 81 (ECF No. 57-1) ("Axelrod Third Rep."); Report, dated June 21, 2021, filed as Ex. 102 (ECF No. 69-1) ("Axelrod Fourth Rep.").

Dr. Axelrod received his undergraduate degree, medical degree, and graduate degree from the University of Michigan. *See* Curriculum Vitae, filed July 23, 2018 (ECF No. 31-2) ("Axelrod CV") at 1; Tr. at 102–3. Dr. Axelrod held several academic appointments throughout his career including Walter Reed Army Institute of Research, Medical College of Ohio, and UMDNJ-New Jersey Medical School. Axelrod CV at 2. Dr. Axelrod was a Principal Investigator at the Walter Reed Army Institute and participated in the study and development of a vaccine. Axelrod CV at 1; Axelrod First Rep. at 1. Before retiring, he worked in private practice as a rheumatologist and allergist at the Allergy and Asthma Center in Maryland, and saw patients with adult autoimmune diseases, allergies, and occasionally immune deficiencies. Axelrod CV at 2; Tr. at 102. As a clinician, Dr. Axelrod diagnosed and treated patients with various drug reactions. Axelrod First Rep. at 1. He is board certified in Internal Medicine, Adult Rheumatology, Medical Laboratory Immunology, and Allergy and Immunology, and has published several articles and abstracts over the course of his career. *Id*.; Axelrod CV at 3–4.

Dr. Axelrod began his testimony with a brief overview of Petitioner's diagnosis, agreeing with Dr. Lovitt that Petitioner had experienced meningoencephalitis—which he in turn proposed was more likely than not vaccine-induced. Tr. at 105–06. He then provided an explanation of the concept of autoimmunity and the role in which molecular mimicry plays in it. Most autoimmune

disorders occur in individuals with a genetic predisposition and/or susceptibility to developing such a disorder. Tr. at 109; Axelrod First Rep. at 2. As a result, Dr. Axelrod deemed it likely that Mr. Tipps possessed some type of susceptibility to developing autoimmune meningoencephalitis. *Id*. at 109–110.

However, Dr. Axelrod explained, while an individual may be predisposed to developing an autoimmune disorder, infectious agents (including counterpart vaccines) can act as principal environmental insults subsequently responsible for the induction of autoimmune disease. Axelrod Second Rep. at 2; M. Cusick & R. Fujinami, *Molecular Mimicry as a Mechanism of Autoimmune Disease*, 42 Clinical Rev. Allery Immunology 102, 102 (2012), filed as Ex. 55 (ECF No. 41-4) (finding proinflammatory cytokines are critical to the clearance of pathogens, and further suggesting that environmental factors can divert the immune response towards immunopathogenesis).

Dr. Axelrod next proposed a theory for how the meningococcal and Tdap vaccines could have caused Petitioner's meningoencephalitis, focusing on the concept of "anti-idiotypic" antibodies becoming pathogenic due to molecular mimicry. Tr. at 112; Axelrod First Rep. at 2–3; Axelrod Second Rep. at 2–3; Axelrod Fourth Rep. at 1, 4–7. When an individual is exposed to some external agent immunologically, a damaging, autoimmune-mediated cross-reaction can occur via molecular mimicry. Tr. at 109–110. This can occur if the various segments of amino acids that make up the external agent (assuming it is viral, and thus protein-based) are sequentially or structurally similar to self-tissue sequences/structures—meaning the immune response to the foreign antigen (whether by producing antibodies, other immune cells (meaning T cell-oriented), or a combination thereof) can react to self, resulting in autoimmune damage and/or excessive inflammation. *Id*. at 110.

In this case, Dr. Axelrod proposed that a specific kind of antibody—anti-idiotypic antibodies—were the pathogenic drivers of this putative autoimmune process. Axelrod First Rep. at 3. Tr. at 112–13. He defined them to be antibodies that can bind to the variable region (or "idiotype") of another antibody, and thus can impact immunogenicity (in potentially good and bad ways). Axelrod First Rep. at 1. Dr. Axelrod specifically proposed that anti-idiotypic antibodies have the ability to attach to aspects of the nervous system in a manner similar to that of the tetanus toxoid, diphtheria toxoid, and fragments A and B of the pertussis toxin, and thereby cause comparable harm. Thus, he theorized that autoimmune meningoencephalitis could be the result of production of anti-idiotypic antibodies in response to vaccination. Tr. at 112.

To support his theory (and in reaction to assertions by Respondent's expert), Dr. Axelrod attempted to first show that the viral toxins/toxoids at issue could themselves give rise to pathology. One article was offered to show that certain subunits of the pertussis toxin can interact with neuronal gangliosides. Axelrod First Rep. at 3; M. Hara-Yokoyama et al., *Identification of*

Gangliosides as Inhibitors of ADP-Ribosyltransferases of Pertussis Toxin and Exoenzyme C3 from Clostridium Botulinum, 270 J. of Biological Chemistry 8115 (1995), filed as Ex. 85 (ECF No. 57-5) ("Hara-Yokoyama"). While Respondent's immunologic expert, Dr. Andrew MacGinnitie, argued (as discussed below) that Hara-Yokoyama only showed that the gangliosides can inhibit the enzymatic activity of the pertussis vaccine, Dr. Axelrod maintained that if the pertussis toxins can bind to the gangliosides, then anti-idiotypic antibodies can also bind to the gangliosides and cause inflammation or damage. Axelrod First Rep. at 3; Axelrod Third Rep. at 2. Thus, Dr. Axelrod reasoned, vaccines containing the pertussis toxin could, like their wild counterparts, cause the production of anti-idiotypic antibodies that could interact with the neuronal ganglioside and cause dysfunction or damage to the neurons.

Dr. Axelrod also attempted to demonstrate how anti-idiotypic antibodies might interact with nerve gangliosides in a pathologic manner. Tr. at 117. He referenced one item of literature that he maintained had found that gangliosides are abundantly expressed within the CNS, constituting roughly 97% of all gangliosides in the human brain. Tr. at 120; K. Vajn et al., *Differential Distribution of Major Bran Gangliosides in the Adult Mouse Central Nervous System*, 8 PLoS ONE 1, 1 (2013), filed as Ex. 86 (ECF No. 57-6) ("Vajn"). Thus, an anti-idiotypic immune response to the pertussis toxoid could produce a direct inflammatory response when interacting with these gangliosides, leading to a damaging inflammatory process. *Id*.; S. Mangmool & H. Krouse, *$G_{i/o}$ Protein-Dependent and -Independent Actions of Pertussis Toxin (PTX)*, 3 Toxins 884, 893 (2011), filed as Ex. 87 (ECF No. 57-7) ("Mangmool") (establishing that the pertussis toxin modifies cellular response by at least two signaling pathways (the A-promoter and the B-Oligomer)); I. Gomes et al., *Neuropeptide Receptors*, 4 Colloquium Series of Neuropeptides 21 (2013), filed as Ex. 88 (ECF No. 57-8) ("Gomes") (finding the highest level of G-protein-coupled receptors (GPCRs) located within the central nervous system). Dr. Axelrod again emphasized that since the components of various toxins—tetanus, diphtheria, or pertussis—were capable of binding to CNS gangliosides, anti-idiotypic antibodies should have the same capacity. Tr. at 117.

Dr. Axelrod then discussed how immune system-produced antibodies (whether they activate, complement, or direct cytotoxic cells to a particular area and respond to a specific antigen or receptor, an inflammatory reaction) could cause either tissue damage or an exacerbation of the inflammation. Tr. at 117. *See also* N. K. Jerne, *Towards a Network Theory of the Immune System*, 125 Annales of Immunology 373, 378 (1974), filed as Ex. 29 (ECF No. 30-4) ("Jerne") (arguing that idiotypes play an important role in understanding immunology because they are determined by the same variable region that determines the antibody binding site); S. Quaglia et al., *A Functional Idiotype/Anti-Idiotype Network is Active in Genetically Gluten-Intolerant Individuals Negative for Both Celiac Disease-Related Intestinal Damage and Serum Antibodies*, 202 J. Immunology 1079, 1081 (2019), filed as Ex. 107 (ECF No. 69-6) ("Quaglia") (relying on the framework set out by Jerne, and finding that the hypervariable region of an anti-idiotype antibody can recognize the hypervariable region of the idiotype and mimic the original antigen). Because the vaccines at issue contain antigens comparable to the wild toxins, anti-idiotypic antibodies

produced in response could essentially "mimic" their wild counterparts (even though that kind of mimicry is not consistent with pure molecular mimicry between a foreign antigen and self-structure).

Dr. MacGinnitie had contended (as discussed below) that anti-idiotype antibodies were more likely to be *protective* against autoimmune conditions, but Dr. Axelrod disagreed, offering additional literature to support his position. *See e.g.*, L. Fernandez et al., *Ganglioside Based Vaccines and Anti-Idiotype Antibodies for Active Immunotherapy against Cancer*, 2 Expert Rev. Vaccines 817, 819–20 (2003), filed as Ex. 94 (ECF No. 58-5) ("Fernandez") (developing an anti-idiotype antibody by creating a monoclonal antibody with the anti-idiotype antibody, and showing that the resulting antibody created an active immune response to damage malignant cells); M. N. Islam et al., *Biological Activity of Anti-Thyrotropin Anti-Idiotypic Antibody*, 13 European J. of Immunology 57, 59–60 (1983), filed as Ex. 75 (ECF No. 43-4) ("Islam") (showing that anti-thyrotropin anti-idiotype antibody can produce findings consistent with Graves Disease).[12]

Dr. Axelrod further addressed the relevance of the blood-brain barrier[13] to his theory. He acknowledged that for CNS injury to occur due to some external agent, the blood-brain barrier would need to be breached. Tr. at 126– 27. Because Mr. Tipps had suffered from an inflammatory response directed to his CNS, it was likely that the disease process had caused an increase of cytokines sufficient to make this breach occur. *Id*. This in turn would lead to the transfer of immune cells and antibodies into the CNS. *See e.g.*, K. Rochfort et al., *Downregulation of Blood-Brain Barrier Phenotype by Proinflammatory Cytokines involves NADPH Oxidase-Dependent ROS Generation: Consequences for Interendothelial Adherens and Tight Junctions*, 9 PLoS ONE, Jul. 2014, at 6 (2014), filed as Ex. 90 (ECF No. 58-1) ("Rochfort") (taking human brain microvascular endothelial cells and exposing them to various concentrations of proinflammatory cytokines, and finding the blood-brain barrier was resultantly more susceptible to opening); Y. Kashiwagi et al., *Production of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type b (Hib), and 7-Valent Pneumococcal (PCV7) Vaccines*, 10 Human Vaccines & Immunotherapeutics 677, 679-80 (2014), filed as Ex. 91 (ECF No. 58-2) ("Kashiwagi") (immunization with DPT resulted in concentration of cytokines in low nanogram

[12] "Graves Disease" is defined as "a syndrome of diffuse hyperplasia of the thyroid, with a female predominance; it usually has an autoimmune etiology and has been linked to autoimmune thyroiditis." *Grave Disease*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=70364&searchterm=Graves+disease (last visited Dec. 9, 2022).

[13] "Blood-brain Barrier" is defined as "the barrier system separating the blood from the parenchyma of the central nervous system. Its anatomic component consists of unique endothelial cells in the brain capillaries, having tight junctions without fenestrations and with few microvilli and few vesicles for fluid transport. Its physiologic component in part consists of enzymes unique to the brain endothelia and of active transport via carrier proteins." *Blood-brain Barrier*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=60232&searchterm=blood-brain+barrier (last visited Dec. 9, 2022).

range—thus, releasing more cytokines and causing the opening of blood-brain barrier); Axelrod Fourth Rep. at 3.

Dr. Axelrod concluded by briefly discussing the timing of Mr. Tipps's symptoms. He agreed with Dr. Lovitt that Petitioner's onset (16 days post-vaccination) was consistent with the timeframe for the development of autoimmune meningoencephalitis after a causal trigger, based on how long he proposed it would take for the anti-idiopathic antibodies to generate. *See* R. Geha, *Presence of Auto-Anti-Idiotypic Antibody during the Normal Human Immune Response to Tetanus Toxoid Antigen*, 129 J. Immunology 139, 139 (1982), filed as Ex. 60 (ECF No. 41-9) ("Geha") (finding, based upon two-patient sample, that immunization with tetanus toxoid-containing vaccine resulted in increase of anti-idiotypic antibodies within a couple of weeks). Dr. Axelrod also noted that Geha demonstrated that where an individual received a booster immunization with tetanus toxoid, anti-idiotypic antibodies could begin to increase within a couple of weeks. Geha at 142. And the vaccines received by Mr. Tipps were also boosters, like those evaluated in Geha. (As later pointed out by Dr. MacGinnitie, however, Geha was published 40 years ago—and has not since been updated by other literature testing its facially-limited findings).[14]

B. Respondent's Experts

1. Dr. Elaine C. Wirrell, M.D., FRCPC

Dr. Wirrell, a pediatric neurologist, testified on behalf of Respondent, and submitted three expert reports. *See generally* Tr. at 164–262; Report, dated Apr. 21, 2020, filed as Ex. C (ECF No. 46-1) ("Wirrell First Rep."); Report, dated Apr. 21, 2020, filed as Ex. D (ECF No. 46-2) ("Wirrell Second Rep."); Report, dated Apr. 21, 2020, filed as Ex. E (ECF No. 46-3 ("Wirrell Third Rep."). Dr. Wirrell largely focused her opinion on the potential impact the vaccinations had on Petitioner, and whether they had any connection with his subsequent neurological symptoms.

Dr. Wirrell obtained her bachelor's degree from Simon Fraser University in Burnaby, British Columbia, followed by her medical degree at the University of British Columbia. *See* Curriculum Vitae, filed as Ex. G (ECF No. 46-5) ("Wirrell CV") at 1; Tr. at 164. Thereafter, she completed a general pediatrics residency and child neurology fellowship at Dalhousie University in Halifax, Nova Scotia. Wirrell CV at 1; Tr. at 165. She has been the Director of Pediatric Epilepsy at Mayo Clinic in Rochester, Minnesota since 2007. Tr. at 165; Wirrell First Rep. at 1. She also serves as the Director of Child and Adolescent Neurology Program Training at Mayo Clinic. *Id.* She is board certified in pediatrics and neurology through the Royal College of Physicians and Surgeons in Canada, which is the equivalent to that of a U.S. certification. *Id*. In addition, she has published over 180 peer-reviewed articles and 20 book chapters, largely focused on pediatric epilepsy and seizure disorders. Wirrell First Rep. at 1.

[14] *See* Report, dated Apr. 16, 2019, filed as Ex. A (ECF No. 37-1) ("MacGinnitie First Rep.") at 7.

Dr. Wirrell began her testimony by stating her medical opinion that the meningococcal and Tdap vaccinations received by Mr. Tipps in July 2013 were not likely related to his meningoencephalitis. Tr. at 168. Rather, based on Mr. Tipp's clinical presentation, his symptoms were most consistent with *viral* meningoencephalitis, denying that the criteria for an autoimmune encephalitis diagnosis had been met. Tr. at 169–70. K. Bloch & C. Glaser, *Encephalitis Surveillance through the Emerging Infections Program, 1997-2010*, 21 Emerging Infectious Diseases 1562 (2015) ("Bloch & Glaser").

Dr. Wirrell discussed at length the broad number of etiologies for meningoencephalitis. Wirrell First Rep. at 13. In particular, she relied on several larger studies that looked at patients who had clearly met the criteria for encephalitis or meningoencephalitis. Tr. at 170; Wirrell First Rep. at 13. Bloch & Glaser, for example, identified a large number (>5,000) of patients with encephalitis, observing that in almost half of all cases there was no identified underlying cause for encephalitis, despite extensive infectious testing. Tr. at 170; Wirrell First Rep. at 13; Bloch & Glaser at 3. A second study had examined 92 adult patients in Italy, finding that two thirds of cases for aseptic central nervous system infections had no clear identifiable etiology. Tr. at 171; Wirrell First Rep. at 13; J. Monticelli et al., *Aseptic Central Nervous System Infections in Adults: What Predictor for Unknown Etiological Diagnosis?*, 39 Neurological Sci. 863, 863 (2018).

Other items of literature reached the same conclusion. *See, e.g.,* B. George et al., *Encephalitis Hospitalization Rates and Inpatient Mortality in the United States, 2000-2010*, 9 PLoS ONE 1, 5 (2014), filed as Ex. C-9 (ECF No. 48-9) ("George") (finding an estimated rate of 7.3 hospitalizations per 100,000 per year with over half of the cases having an unidentified cause of etiology); K. DuBray et al., *Epidemiology, Outcomes and Predictors of Recovery in Childhood Encephalitis: A Hospital-based Study*, 32 Pediatric Infectious Disease J. 839, 843 (2013), filed as Ex. C-4 (ECF No. 48-4) (concluding that of 190 children admitted to a single California hospital for encephalitis, roughly half of the children studied did not have an identified cause of etiology). Moreover, where an etiology has been found, the most common (according to Dr. Wirrell) is infectious. Wirrell First Rep. at 13.

Dr. Wirrell further disputed that the record supported a diagnosis of *autoimmune* encephalitis. The most common form of an autoimmune encephalitis, she maintained, is "NDMA receptor encephalitis."[15] But even in the absence of antibody testing (then-available in 2013) from this case that would confirm the presence of the autoantibodies understood to drive that disease, Mr. Tipps's clinical presentation was inconsistent with it. Tr. at 178. Children with NMDA

[15] "Anti-NDMA Receptor Encephalitis" is defined as "an autoimmune disease where the body creates antibodies against the NDMA receptors in the brain. These antibodies disrupt normal brain signaling and cause brain swelling or encephalitis." *Anti-NDMA Receptor Encephalitis*, Center for Autoimmune Neurology, Pearlman School of Medicine, University of Pennsylvania, https://www med.upenn.edu/autoimmuneneurology/nmdar-encephalitis html (last visited Dec. 9, 2022).

receptor encephalitis typically experience pronounced psychosis and hallucinations, later developing other symptoms such as motor dyskinesias[16] and (in many cases) seizures—clinical features that both sides' diagnostic experts agreed were mostly absent from the record. *Id* at 179. The second most common type of autoimmune encephalitis, "Acute Disseminated Encephalomyelitis (ADEM)," usually presents with multifocal numbness, visual loss, ataxia, and tremors. *Id*. at 180. And MRI readings for ADEM typically show multifocal T2 or flare hyperintense lesions. *Id*.

Mr. Tipps's MRI findings, however, were inconsistent with autoimmune encephalitis. Tr. at 182. Dr. Wirrell recalled that Mr. Tipps had two MRIs—the first on August 29, 2013, and the second on September 12, 2013—both of which showed a relatively small T2 hyperintensity. *Id.* Such findings were more likely the result of gliosis, scarring, or a slightly larger perivascular space around one of the blood vessels. *Id*. Had Mr. Tipps been suffering from an autoimmune form of encephalitis, Dr. Wirrell opined, the T2 hyperintensities would not only be larger in size but would also be accompanied by pronounced contrast—which the MRIs did not indicate. *Id*. Moreover, Dr. Wirrell noted that she would have expected Mr. Tipps's first MRI to show more enhancement due to his elevated cell count (consistent with the presence of significant inflammation), but the fact that it did not actually reduced the likelihood of an autoimmune encephalitis. *Id*.

Dr. Wirrell also reiterated the difference between meningitis and encephalitis as articulated by Dr. Lovitt in his testimony, emphasizing the extent to which the medical record *did* contain evidence of symptoms associated with both. Tr. at 174. Encephalitis would generally present with behavioral changes, seizures or other focal neurological findings, and there was support in the record for Petitioner experiencing some of these symptoms. *Id*. Meningitis generally features headache, occasional neck stiffness or neck, pain, vomiting, and an elevation in CSF white count—which Mr. Tipps presented with. *Id*. In addition, Mr. Tipps's cerebrospinal fluid taps were more indicative of viral meningoencephalitis rather than bacterial meningoencephalitis, which would feature a very high white cell count, low glucose level, and high protein level. *Id*. at 175–76.

Dr. Wirrell then discussed the steroid treatments Mr. Tipps received throughout his various hospitalizations, explaining why she believed such treatments were further evidence that Mr. Tipps suffered from viral form of meningoencephalitis. Tr. at 184. The medical records indicated that Mr. Tipps's white blood cell count had significantly decreased before his treating physicians started him on steroids—suggesting that any infectious process at work was beginning to resolve on its own. *Id*. By August 19, 2013, Mr. Tipps's WBC was 163, and by September 9, 2013, his WBC had decreased to 43—thus, keeping more in line with a viral meningoencephalitis. *Id*. The

[16] "Dyskinesia" is defined as "distortion or impairment of voluntary movement, as in tic, spasm, or myoclonus." *Dyskinesia*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=15221 (last visited on Dec. 9, 2022).

purpose of the steroidal treatment was likely more to address Petitioner's significantly increased intracranial pressure, and the fact that he was beginning to lose his vision. *Id*.

Relying on several studies, Dr. Wirrell also briefly addressed the relationship between vaccination and encephalopathy. Tr. at 188–89. One article had evaluated patients who presented with encephalopathy or encephalitis following the Tdap vaccination. S. Chang et al., *U.S. Postlicensure Safety Surveillance for Adolescent and Adult Tetanus, Diphtheria and Acellular Pertussis Vaccines: 2005-2007*, 31 Vaccine 1447 (2013), filed as Ex. C-3 (ECF No. 48-3) ("Chang"). Of the 20 million doses given to these patients, there were roughly 2,000 reports of patients who reportedly presented with encephalopathy or encephalitis. Wirrell First Rep. at 11; Chang at 1448. However, after a more in-depth review, only *three* of the reports were suggestive of encephalopathy or encephalitis, and thus Chang's findings were not consistent with the conclusion that vaccination could lead to encephalopathy. *Id.* at 1450–51.

Another study sought to determine the expected rate of persons developing encephalopathy, encephalitis, or meningitis post-vaccination as opposed to the observed rate following receipt of the Tdap vaccine. W. Yih et al., *An Assessment of the Safety of Adolescent and Adult Tetanus-Diphtheria-Acellular Pertussis (Tdap) Vaccine, using Active Surveillance for Adverse Events in the Vaccine Safety Datalink*, 27 Vaccine 4257 (2009), filed as Ex. 70 (ECF No. 42-9) ("Yih"). But Yih determined that the observed rate specific to the Tdap vaccine was in fact *lower* than the expected rate. Yih at 4257, 4262; Tr. at 191. *See also* T. Nakayama & K. Odona, *Vaccine Adverse Events Reported in Post-Marketing Study of the Kitasato Institute from 1994 to 2004*, 25 Vaccine 570, 574 (2007), filed as Ex. 71 (ECF No. 42-10) ("Nakayama") (reporting only *one* case of encephalitis/encephalopathy out of 10.56 million doses of DPT); M. Griffin et al., *Risk of Seizures and Encephalopathy after Immunization with the Diphtheria-Tetanus-Pertussis Vaccine*, 263 J. Am. Med. Ass'n., 1641, 1643 (1990), filed as Ex. 73 (ECF No. 43-2) ("Griffin") (reporting the hospitalization of two children following receipt of the DPT vaccination (and hence a different version of the Tdap vaccine), but concluding that neither had permanent sequalae and were thus not further considered in the study).

In response to Petitioner's expert's proposal that molecular mimicry induced by the Tdap and meningococcal vaccinations caused Mr. Tipp's encephalitis and neurological symptoms, Dr. Wirrell emphasized that there was only a single report of *autoimmune* encephalitis being temporally related to a vaccine comparable to what Petitioner had received. Wirrell Second Rep. at 2; C. Hofmann et al., *Anti-NMDA Receptor Encephalitis after TdaP-IPV Booster Vaccination: Cause or Coincidence?*, 258 J. Neurol. 500 (2011), filed as Ex. C-14 (ECF No. 48-14) ("Hofmann") (finding a 15-year old had developed a fever within 24-hours post-vaccination which progressed to NMDA-receptor encephalitis—and while this association could not be assumed, it might be coincidental). And Hoffman did not even involve the form of injury that Dr. Wirrell opined was most likely at issue.

Dr. Lovitt had offered a different study which he maintained reliably established that cases of encephalitis were still observed following the introduction of the acellular pertussis-containing vaccine (which replaced whole cell pertussis for safety reasons). H. Kuno-Sakai & M. Kimura, *Safety and Efficacy of Acellular Pertussis Vaccine in Japan, Evaluated by 23 Years of its use for Routine Immunization*, 46 Pediatrics Int'l 650, 654 (2004), filed as Ex. C-16 (ECF No. 48-16) ("Kuno-Sakai"); Wirrell Second Rep. at 2. Kuno-Sakai reported a rate of approximately 1.3 cases of encephalitis per 10 million children within seven days of receiving the acellular pertussis containing vaccine. *Id*. However, Dr. Wirrell argued that in order to determine whether there is any epidemiological evidence to support a causal relationship between vaccination and encephalitis, a comparison must be done between the *baseline* rate of encephalitis in a population overall, versus what is seen following vaccination. Tr. at 188; Wirrell Second Rep. at 2; Wirrell Third Rep. at 4. Two large national studies conducted in the U.S. and the U.K. actually revealed that the baseline rate of post-vaccination encephalitis reported in the Kuno-Sakai article was significantly *lower* than the baseline rates for the general population. Tr. at 187; Wirrell Second Rep. at 2; J. Granerod et al., *New Estimates of Incidence of Encephalitis in England*, 19 Emerging Infectious Diseases 1455 (2013), filed as Ex. C-10 (ECF No. 48-10) ("Granerod") (finding an estimated rate of 5.23 cases of encephalitis per 100,000 per year in the U.K.); George at 5 (U.S. study). Thus, existing epidemiologic evidence suggested *less* risk of encephalitis among the vaccinated population—not more.

Dr. Wirrell was not otherwise asked to comment directly on Dr. Axelrod's theory of causation, deferring to Dr. MacGinnitie. Tr. at 196. But she did state that in her own clinical background and experience, she had never come across anything supporting a relationship between anti-idiotype antibodies and autoimmune encephalopathy. *Id*.[17]

2. Dr. Andrew J. MacGinnitie, M.D.

Dr. MacGinnitie, an attending physician and the Clinical Director for the Division of Immunology at Boston's Children's Hospital, testified on behalf of Respondent, and submitted three expert reports. *See generally* Tr. at 264–337; Report, dated Apr. 16, 2019, filed as Ex. A (ECF No. 37-1) ("MacGinnitie First Rep."); Report, dated, Apr. 21. 2020, filed as Ex. F (ECF No.

[17] Dr. Wirrell also responded at some length in her reports to the "Miller" Criteria proposed by Dr. Axelrod as bearing on whether causation can be demonstrated as a general matter of science. Wirrell Third Rep. at 2; F. Miller et al., *Approaches for Identifying and Defining Environmentally Associated Rheumatic Disorders*, 43 Arthritis & Rheumatism 243, 244 (2000), filed as Ex. 58 (ECF No. 41-7) ("Miller"). In this regard, she contested Dr. Axelrod's opinion as to the Miller Criteria elements one (temporal association), two (lack of alternative explanation), and five (biologic plausibility). Tr. at 195-96; Wirrell Third Rep. at 2–3. She also observed that Dr. Axelrod did not discuss in detail several of the elements. Tr. at 194; Miller at 245. I do not, however, include further discussion of this aspect of the competing expert opinions, for the simple reason that causation is determined by a legally-derived test, rather than by factors deemed persuasive *in science* (even though ultimate medical or scientific *reliability* is very important in assessing causation).

46-4) ("MacGinnitie Second Rep."); Report, dated May 14, 2021, filed as Ex. H (ECF No. 65-1) ("MacGinnitie Third Rep."). Dr. MacGinnitie argued that the cause of Mr. Tipps's meningoencephalitis was unrelated to the Tdap and Meningococcal vaccines he had received. Tr. at 268.

Dr. MacGinnitie received his bachelor's degree from Yale University and then attended the University of Chicago, Pritzker School of Medicine, where he received both an M.D. and a Ph.D. from the Department of Pathology. *See* Curriculum Vitae, filed as Ex. B (ECF No. 37-2) ("MacGinnitie CV"); Tr. at 264. He completed a residency in pediatrics in the Boston Combined Residency Program, a joint venture of Boston Children's Hospital and Boston Medical Center, followed by an Allergy/Immunology fellowship at Boston Children's Hospital. MacGinnitie CV at 1; Tr. at 264; MacGinnitie First Rep. at 1. He is board certified in both Pediatrics and Allergy and Clinical Immunology. Tr. at 266; MacGinnitie First Rep. at 1. Dr. MacGinnitie has also published several articles in areas related to Allergy/Immunology, such as food allergy and vaccine reactions. MacGinnitie First Rep. at 1.

Dr. MacGinnitie began by discussing anti-idiotype antibodies generally. MacGinnitie First Rep. at 3. He maintained that while "theoretically appealing [,] there is little data regarding the actual importance of anti-idiotype antibodies in human disease." Tr. at 268–69; MacGinnitie First Rep. at 4. Thus, he questioned whether it was credible to argue in the first place that this kind of antibody could even be *pathogenic*—let alone be produced in reaction to the vaccines in question. Tr. at 269.

Dr. MacGinnitie next scrutinized the steps implicit in Dr. Axelrod's theory, noting how at each stage there were evidentiary deficiencies. Tr. at 269–70; MacGinnitie Second Rep. at 2. Dr. MacGinnitie first disputed the contention that tetanus, pertussis, and diphtheria toxins could bind to neuronal tissues. *Id*. He contended that Dr. Axelrod had provided little to no evidence that the binding causes pathology, but instead only offered evidentiary support for the idea that more generally vaccine *components* can bind to neuronal tissues or gangliosides. *Id*. And the distinction between the *toxoids* included in vaccines and their predicate toxins was highly relevant to why Dr. MacGinnitie took issue with this aspect of Dr. Axelrod's theory. As Dr. MacGinnitie explained, "in the case of diphtheria, pertussis, and tetanus, they all express toxins that can lead to different illnesses [a]nd *because the toxins cause illness* it [is] not advisable to vaccinate with the toxins themselves." Tr. at 270 (emphasis added). By contrast, a toxoid based on a toxin is either denatured or undergoes an altered protein sequence before being included in a vaccine, greatly reducing (if not eliminating) the risk of a pathologic reaction in any way comparable to a toxin. *Id*.

Moreover, Dr. MacGinnitie criticized several of the articles relied upon by Dr. Axelrod to show the pathogenic capability of the toxins/toxoids, arguing that the data generated or relied upon by these articles was not only outdated but irrelevant to the circumstances in this case. Tr. at 271–

73. Hara-Yokoyama, for example, at best established that the pertussis toxin has the capability of interacting with neuronal tissues which can then lead to dysfunction and damage to the effected neurons. MacGinnitie Second Rep. at 2; Yokoyama at 8118. But that study was not only based on data that is nearly 30 years old, but its ultimate finding was more limited: that pertussis toxin can cause *inhibition* of neuronal tissues and gangliosides, not that the toxin itself *directly binds or damages* the neuronal tissues. Tr. at 271; MacGinnitie Second Rep. at 2. And Hara-Yokoyama otherwise shed no light on the impact the pertussis toxoid would have on a human, and/or in an *in vivo* context. Tr. at 271. He made a comparable point in reaction to other items of literature offered by Dr. Axelrod. *See also* Tr. at 272; MacGinnitie First Rep. at 5; MacGinnitie Second Rep. at 2. Vajn talks about distribution of brain gangliosides in the mouse brain, but does not deal with binding to toxins in vaccines. Tr. at 272. Gomes explores how different neuropeptide receptors are expressed throughout brain, but says nothing about toxins. *Id.* at 272–73. And Mangmool only focused on how the pertussis toxin can act on G-proteins, without expanding to the anticipated effect of the more-relevant toxoids included in the vaccines Petitioner received. *Id*. at 273.

Dr. MacGinnitie then discussed the third component of Dr. Axelrod's theory—that the immune system could (in reaction to vaccination) generate destructive anti-idiotypic antibodies, maintaining that evidence relied upon for the point was not only speculative but outdated. Tr. at 270; MacGinnitie Second Rep. at 2–3. Jerne, for example, was largely theoretical in nature, with its authors only speculating as to the importance of anti-idiotype antibodies, but providing no actual data establishing any relevance to human disease. Tr. at 274; MacGinnitie Second Rep. at 3; Jerne at 378. Moreover, the contemporaneous evidence that does exist regarding anti-idiotype antibodies and autoimmune diseases suggests that the antibodies are more *protective* than they are *causative*. Tr. at 275; MacGinnitie First Rep. at 7; MacGinnitie Second Rep. at 5. Jerne was otherwise 44 years old, and its suggestions had not been subsequently updated to show that "anti-idiotype antibodies are involved in human disease or CNS inflammation." MacGinnitie First Rep. at 6.

Next, Dr. MacGinnitie discussed the articles cited by Dr. Axelrod to demonstrate a pathogenic effect of anti-idiotypic antibodies in causing encephalomyelitis. Tr. at 276–81; MacGinnitie Second Rep. at 4. Islam, for example, was an animal model in which rabbits were immunized with anti-TSH antibodies, an artificial solution, finding that the resulting antibodies could trigger symptoms similar to Graves disease. Tr. at 277; MacGinnitie Second Rep. at 4; Islam at 57. But other than being an immune system disorder, there was nothing about Graves disease making it comparable to encephalitis of the kind Petitioner was believed to have experienced. Similarly, another article that featured an animal model with one human patient aimed to demonstrate the relationship between anti-idiotype antibodies and autoimmune diseases such as myasthenia gravis and Graves disease. Tr. at 278; B. F. Erlanger et al., *Auto-Anti-Idiotype: A Basis for Autoimmunity and a Strategy for Anti-Receptor Antibodies*, 94 Immunological Reviews 23, 35 (1986), filed as Ex. 93 (ECF No. 58-4) ("Erlanger"). But Dr. MacGinnitie maintained that Erlanger

involved an artificial solution (purifying the antibody against a particular compound found in myasthenia gravis) and thus showed no relation to the vaccines at issues. Tr. at 278. And Fernandez focused on antibodies against cancer cells, as opposed to antibodies causing brain injury. Dr. MacGinnitie also emphasized the stale nature of the data reviewed, maintaining that if there were likely anti-idiopathic antibodies involved in myasthenia gravis or Graves disease, more data would have come out by now. Tr. at 278–79.

Another deficiency Dr. MacGinnitie identified in Petitioner's theory was its failure to establish how the putatively-harmful anti-idiotypic antibodies would likely cross the blood-brain barrier (which they would need to do to cause harm). Tr. at 287; MacGinnitie Second Rep. at 3. Antibodies are generally excluded from the CNS as a result of the protective effect of the blood-brain barrier; indeed, Dr. MacGinnitie noted, this is why it is difficult to employ antibody therapies for treating various CNS diseases. *Id*; I. Amanna & M. Slifka, *Contributions of Humoral and Cellular Immunity to Vaccine-Induced Protection in Humans*, 411 Virology 206, 212 (2011), filed as Ex. F-6 (ECF No. 47-6). Thus, it was unlikely anti-idiotype antibodies produced by the pertussis, diphtheria, and tetanus toxins could "get through" to cause damage to the CNS. Tr. at 287; MacGinnitie Second Rep. at 3. Moreover, in the case of Mr. Tipps, Dr. MacGinnitie observed no evidence in his clinical presentation to suggest a breach in the blood-brain barrier had occurred. *Id*.

Dr. MacGinnitie allowed, however, that there are limited exceptions where the blood-brain barrier is breached by antibodies, and in so doing he addressed whether cytokines produced in response to vaccines could contribute to such circumstances. Tr. at 287. He agreed that vaccinations *do* generate cytokines, but argued that there was no evidence in Mr. Tipps's clinical presentation to suggest that he had experienced any significant elevation of cytokines. Tr. at 288; Kashiwagi at 679, 683 (arguing that "all effective vaccines induce the production of cytokines or chemokines, which modulate immunogenicity and are also involved in inducing adverse events, such as systemic febrile illness and immunotoxicity"). Thus, Mr. Tipps exhibited no symptoms (such as fever, local soreness, etc.) preceding the onset of his injury that would reflect excessive cytokine upregulation. Another of Petitioner's items of literature, Rochfort, was offered to show that cytokines at nanogram levels having the ability to "disrupt the expression of certain adhesion molecules on human brain endothelial cells," in turn resulting in the opening of the blood-brain barrier. MacGinnitie Third Rep. at 3; Rochfort at 2. But Dr. MacGinnitie disputed whether Rochfort's *in vitro* results were meaningful when applied to an *in vivo* context. Tr. at 291; MacGinnitie Third Rep. at 4.

Dr. MacGinnitie then discussed several articles he relied on to demonstrate that the Tdap vaccine is not linked with CNS inflammation. Tr. at 292–93. MacGinnitie First Rep. at 6. He referred to a 1991 report cited by Dr. Lovitt in favor of causality, but noted that the report examined the *whole-cell* pertussis vaccine, which Mr. Tipps did not receive. Tr. at 292; MacGinnitie First Rep. at 6; L. Cowan et al., *Acute Encephalopathy and Chronic Neurological Damage after*

Pertussis Vaccine, 11 Vaccine 1371, 1374 (1993), filed as Ex. 16 (ECF No. 25-1) (finding that DPT immunization was associated with an increased risk of seizures and encephalopathy within seven days following receipt of the vaccine). More recent studies suggested no causal relationship had *ever* existed with respect to the whole cell pertussis vaccine version, or the current acellular version. MacGinnitie First Rep. at 6; P. Ray et al., *Encephalopathy after Whole-Cell Pertussis or Measles Vaccination: Lack of Evidence for a Causal Association in a Retrospective Case-Control Study*, 25 The Pediatric Infectious Disease J. 768, 773 (2006), filed as Ex. A-9 (ECF No. 38-9) (relying on an evaluation of two million vaccinated children, no increased risk of encephalopathy after the DTP and MMR vaccinations found); W. Huang et al., *Lack of Association Between Acellular Pertussis Vaccine and Seizures in Early Children*, 126 J. of the Am. Acad. of Pediatrics 263, 266 (2010), filed as Ex. A-10 (ECF No. 38-10) (observing no increased risk in seizures after receipt of the Tdap vaccine); L. Rorke-Adams et al., *Neuropathology of Vaccination in Infants and Children*, 29 Vaccine 8754, 8758 (2011), filed as Ex. A-11 (ECF No. 38-11) (finding the pathogenesis of the majority of the 37 infants/children studied was apparent, and thus not a complication of the vaccination).

Dr. MacGinnitie concluded with a brief response to Dr. Axelrod's contention that the vaccines Petitioner received could cause production of cross-reacting anti-idiopathic antibodies due to molecular mimicry between the vaccine antigens and self, denying that the theory was persuasive. Tr. at 294-295. Dr. MacGinnitie argued that in order to have an autoimmune disease, a target of autoimmunity is needed, which had not been established at all in this case by Petitioner's experts. *Id*. at 295. Moreover, Dr. MacGinnitie emphasized, there was overall a lack of evidence presented by Petitioner's experts to support the notion of cross-reactivity or that autoimmunity is triggered by a vaccine component. *Id*. He also (parallel with Dr. Wirrell) observed a lack of evidence that Mr. Tipps had experienced an autoimmune process. He was in fact never tested for any of the antibodies thought to be associated with autoimmune meningoencephalitis—because his providers did not feel it was necessary based on his clinical presentation. *Id*.

III. Procedural History

As noted above, this claim was initiated in early 2017, approximately five years ago, and assigned to a different special master. Petitioner filed medical records thereafter with the statement of completion filed in May 2017. (ECF No. 17). Respondent's Rule 4(c) Report was filed on July 19, 2017. (ECF No. 19). Expert reports were next filed over the course of the ensuing four years. The case was eventually reassigned to me in July 2020, and I held a status conference with the parties, proposing a schedule for a two-day Entitlement Hearing to be held. The trial was originally scheduled in June 2021, but was subsequently canceled and then rescheduled for the spring of 2022. The claim is now ripe for resolution.

IV. Applicable Legal Standards

A. *Petitioners' Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[18] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*, 418 F.3d at 1278: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

[18] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof" (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly

trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are

contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral or written testimony (provided in the form of an affidavit or declaration) may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any

norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs.*, No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, No. 2015–5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence

in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

ANALYSIS

The parties seem to agree that meningoencephalitis is the proper diagnosis, although they disputed whether Petitioner's illness had a viral or autoimmune etiology. The record does not permit me to conclude a virus was likely causal. Although Dr. Wirrell made several convincing points about why she favored such an etiology (including the important fact that this illness more often than not has a viral cause), test results never *affirmatively* identified any virus, and Petitioner and his father persuasively testified that there was no evidence Mr. Tipps was ill around the time of his onset (although this does not rule out a viral cause that simply was not identified—consistent with an idiopathic etiology). At the same time, however, Respondent far more compellingly established the low likelihood that Petitioner's meningoencephalitis was autoimmune in character—given the absence of confirming test results from the record—MRI imaging, an inconsistent clinical presentation, and a lack of confirmation Petitioner possessed *any* known autoantibodies associated with autoimmune forms of the disease, including the allegedly-causal anti-idiotypic antibodies.

But the case turns on a more fundamental point: Petitioner's experts did not preponderantly establish that "more likely than not" meningoencephalitis *could* be caused by the Tdap or meningococcal vaccines (with Dr. Axelrod's focus far more on the former vaccine than the latter).[19]

Petitioner's causation theory foundered in three primary respects. First, it relied on the mostly-novel theoretical conception (albeit one Dr. Axelrod has unsuccessfully advanced in at least one other recent case)[20] that anti-idiotypic antibodies could be pathologic drivers of

[19] Because a vaccine injury claim must satisfy all three *Althen* prongs (meaning that an inability to satisfy one prong is fatal to the entire claim), I do not discuss Petitioner's success in establishing the third "timeframe" prong. At most, I will observe that cases relying on vaccine-induced antibody production as driving an autoimmune process often succeed where, as here, the span between vaccination and onset is within three weeks. But that does not assist Petitioner if (as I am finding) the evidence does not *also* preponderate in favor of a conclusion that the vaccine *can* result in production of antibodies leading to disease in the first place.

[20] Dr. Axelrod proposed a comparable theory involving the purportedly-pathologic impact of anti-idiotypic antibodies in an admittedly slightly-different context—a significant aggravation claim alleging that the varicella vaccine worsened a petitioner's preexisting peripheral neuropathy. But the theory was rejected. *See generally Pavan v. Sec'y of Health & Hum. Servs.*, No. 14-60V, 2020 WL 5351332 (Fed. Cl. Spec. Mstr. July 28, 2020) (denying compensation). The special master's determination therein was based on an extensive evaluation of the theory and its bases, including articles like Jerne. *Pavan*, 2020 WL 5351332, at *12. The *Pavan* special master ultimately found that the theory "does not adequately explain how the id/anti-idiotype mechanism generates an immune response" that could have produced the complained-of autoimmune disease. *Id.* at *18. In addition, *Pavan* noted that Dr. MacGinnitie (Respondent's expert in that case) persuasively established that the anti-idiotype antibodies were more likely

autoimmune disease. But this theory (which, despite the fact it has not been advanced in the Program often, ironically appears to arise from fairly stale items of literature, like Jerne or Geha) seems mostly to have been proposed out of a desire to provide some link between vaccine components and an autoimmune process. It otherwise lacks needed substantiation on several fronts.

Thus, Dr. Axelrod's theory assumes (incorrectly) that wild infectious toxins would function the same as toxoids included in the Tdap vaccine (expressly *because* they are less likely to cause harm, while still having a beneficial immunologic effect), and that the toxins themselves had a pathologic capacity specific to the injury at issue. It provides little reliable support for the conclusion that the vaccines would cause the production of any of the proposed antibodies deemed pathologic. And it seems to presume that invocation of the concept of molecular mimicry (certainly a scientifically-reliable theory that *in other cases* provides a sound causation explanation) is enough to prevail. *See Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *26 (Fed. Cl. Mar. 23, 2018) (stating that "when attempting to establish a causal mechanism, "[p]etitioners cannot simply invoke the concept of molecular mimicry and call it a day"). How the Tdap vaccine antigens would mimic CNS ganglioside structures sufficient to cause the production of the anti-idiotypic antibodies remains no more than *plausibly* established—and in a loosely sketched manner at that.

Second, the causal theory is also deficient on the "back end" of any putative autoimmune process, because insufficient reliable evidence was offered to establish that a pathologic autoimmune process resulting in meningoencephalitis would likely occur *even if* the Tdap vaccine could cause the production of anti-idiotypic antibodies. As a threshold matter, Dr. MacGinnitie made a number of persuasive points about the great difficulty any antibodies would have in breaching the blood-brain barrier that were not persuasively addressed by Dr. Axelrod. But assuming away this hurdle, Petitioner's experts did not reliably establish how the proposed anti-idiotypic antibodies would instigate the kind of harm needed to result in meningoencephalitis. Thus, the target of the proposed autoimmune attack is unidentified (or merely assumed to be the same as the toxin's purported attack—even though the toxin is not comparable for present purposes to the toxoid actually in the vaccine, nor was it shown likely to bind as proposed). The theory also assumes a cross-reaction driven by a kind of antibody that Dr. MacGinnitie persuasively established is more likely *protective*. And other than some case reports relying on temporal associations—reports that should be weighed against much larger studies (cited by Dr. Wirrell) based on greater amounts of passive surveillance reporting and which show no likely relationship—little reliable evidence has been offered to associate the Tdap vaccine with

regulatory (and in a beneficial sense) of the immune response, and that much of the scientific authority offered in support of the theory was quite old. *Id.* at *19-20.

meningoencephalitis. *Compare* Hoffman *with* George and Granerod; *see also* Chang, Yih, Nakayama, and Griffin.[21]

Finally, the overall theory offered by Dr. Axelrod is facially strained. At bottom, Petitioner's theory posits that because vaccines implicate an immune response, they can plausibly cause autoimmune disease—and then the theory looks for ways to reverse engineer support for that concept. But it is not even evident that *all* forms of encephalitis are autoimmune in character. Certainly, the kinds of autoimmune encephalitis discussed by Dr. Wirrell, like ADEM or Anti-NMDA encephalitis, are not what Petitioner experienced. To argue that his meningoencephalitis *must* be autoimmune simply because it post-dated vaccination is to engage in the kind of *post hoc ergo propter hac* reasoning long rejected in the Vaccine Program. *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *9 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied,* 64 Fed. Cl. 19 (2005), *aff'd*, 451 F. 3d 1352 (Fed. Cir. 2006).

My determination is also somewhat based on the reliability and persuasiveness of the expert opinions, as reflected in the written reports both sides filed and testimony offered herein. Respondent's experts were overall not only clearer in their explanations for the deficiencies they identified in Petitioner's theory, but did a better job in *explaining* those deficiencies through their live testimony, with far more precision and clarity. Petitioner's experts certainly possessed the foundational expertise needed to offer the opinions they did, but they could not breathe life into them simply through their embrace of the opinions proposed. This was especially so with respect to the opinions and testimony of the two immunologists in this case. Dr. MacGinnitie persuasively and thoroughly rebutted Dr. Axelrod's opinion.

[21] Petitioner cannot persuasively shield his theory from such criticism by invoking the rarity of vaccine injuries, or the relative paucity of evidence pertaining to the mysteries of the immune system, to excuse the limited evidence offered herein in support of his theory. As the Court has recognized, "the standard of proof does not operate as a sliding scale that varies depending upon the quantity and quality of the scientific evidence that is available." *Caves v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 119, 143 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012).

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioner has not made such as showing, and is therefore not entitled to compensation. I make this determination despite my strong sympathy for Mr. Tipps's experience in dealing with his illness.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[22]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[22] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.